PEGGY GREB (K10563-2)

Vitamin D Research: Humans May Benefit From Animal Health Studies

Jersey cows are used to study milk fever and other metabolic diseases at the National Animal Disease Center.

Research on how vitamin D can help fight a cattle disease seems to have paid off in recent gains in both beef quality and human health care.

In the latter case, a metabolite of vitamin D's least toxic form, vitamin D_2, is being examined as a potential cancer fighter. In the other, the vitamin's toxic characteristics are being used to tenderize beef.

Both developments can be traced to ARS physiologist Ronald Horst, who for 25 years has studied various vitamins' disease-fighting qualities. He heads the Periparturient Diseases of Cattle Research Unit, part of the National Animal Disease Center in Ames, Iowa.

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Physiologist Ronald Horst prepares a tray of cow plasma extracts to be analyzed for vitamin D by high-pressure liquid chromatography.

Shortly after arriving at Ames in the late 1970s, Horst saw that vitamin D's crucial role in calcium production warranted attention as a possible way to prevent hypocalcemia, or milk fever, in dairy cows. The disease afflicts animals as they produce colostrum, or mothers' first milk. They cannot replace the great quantities of calcium lost in the process.

"This causes them to lose nerve and muscle function, including the ability to stand," Horst says. "They eventually lapse into a coma if not treated." Horst says milk fever affects 6 to 8 percent of all U.S. dairy cows and costs $210 million in losses annually.

Vitamin D_3—the form found in humans and other animals—can prove toxic if too much is given. But, says Horst, "We knew from previous work that high levels of vitamin D_2 could prevent milk fever." So Horst further examined how the less toxic vitamin D_2 worked to prevent the bovine illness. Found mainly in plants, vitamin D_2 is used as a dietary supplement.

"We looked at the blood to see what metabolites were being produced as a result of its consumption. We noticed some metabolites that had not been previously identified," he says. Among them was an active metabolite known as 1,24-dihydroxyvitamin D_2. "By active, we mean it was enhancing calcium absorption and bone calcium resorption," says Horst. That active metabolite became the focus of his studies.

Prevents Growth of Cancer Cells...

For vitamin D to help build strong, healthy bones and teeth, it must be activated, usually into a form, or metabolite, called 1,25-dihydroxyvitamin D_2. But the discovery of 1,24-dihydroxyvitamin D_2 represents a new pathway for vitamin D_2 activation.

Both 1,24-dihydroxyvitamin D_2 and 1,25-dihydroxyvitamin D_2 act in the intestine and kidney to raise blood calcium. Without vitamin D, bones can become thin, brittle, soft, or misshapen. If this vitamin D activation system breaks down, metabolic diseases such as milk fever in dairy cattle and osteoporosis in people can flourish.

In Horst's early studies, 1,24-dihydroxyvitamin D_2—despite showing promise as a less toxic form of vitamin D for replenishing lost calcium in cattle—proved problematic. "It was hard to produce, very expensive, and created some unwanted side effects," says Horst. "As a result, we moved on to other things."

But a few years later, a private pharmaceutical firm began taking a good, long look at 1,24-dihydroxyvitamin D_2 for potential benefits to human health.

Various independent studies have suggested that vitamin D can treat or prevent cancer. "It prevents growth of cancer cells," says Horst. But its toxicity hampered this research.

Excessive intake of vitamin D can lead to anorexia, nausea, vomiting, weakness, nervousness, and impaired renal function, as well as calcification of blood vessels and kidneys. That is why 1,24-dihydroxyvitamin D_2 was attractive to researchers.

"It has a good safety profile," says Joyce Knutson, director of preclinical research at Bone Care International, Inc., based in Madison, Wisconsin. "When you are using a form of vitamin D to fight cancer, you don't want its elevating effect on calcium to create a problem."

She says LR-103, which is 1,24-dihydroxyvitamin D_2's pharmaceutical name, will enter clinical trials for its effect on a variety of cancers before year's end. Bone Care and ARS share a patent on the drug.

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Technician Duane Zimmerman analyzes plasma samples from cows for calcium concentration with an atomic absorption spectrophotometer.

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Ronald Horst collects blood from a Jersey cow to analyze her vitamin D and calcium status.

...And It Tenderizes Meat

Vitamin D's toxicity was used in a positive way in studies conducted with Iowa State University in Ames, which were led by Donald Beitz, a professor of animal science and biochemistry. This research is now being evaluated within the U.S. beef industry.

"We took advantage of the potential toxic effect of vitamin D, and of vitamin D_3 in particular," says Horst. The result: a new way to tenderize beef.

Horst explains that if animals receive too much vitamin D, their blood calcium levels can rise to 40 to 50 percent above normal. "If blood calcium remains at these concentrations for several days, animals can become sick and eventually die," he says. "But most mammals can tolerate an increase in blood calcium of 20 to 30 percent for 3 to 5 days without any harm.

"Creating that 20- to 30-percent elevation in blood calcium by feeding excess vitamin D_3 2 to 3 days before slaughter results in greater muscle calcium and more tender cuts of meat," he says. "Elevated calcium in the meat activates postmortem muscle enzymes that can help degrade structural proteins responsible for tough meat."

He says the method triggers no ill effect for consumers and has no harmful effect on the animal, unless too much vitamin D_3 is used. ARS and Iowa State University share a patent on this technique, which is being tested by private firms. Interest has increased in the past 2 years.

An identical method has been applied to pork. It has led to improved meat color, but no tenderizing effect has been observed.—By **Luis Pons,** ARS.

This research is part of Animal Health, an ARS National Program (#103) described on the World Wide Web at www.nps.ars.usda.gov.

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